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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/604,340	07/13/2003	Markus Hildinger	2	1339

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MARKUS HILDINGER
TIGEM
VIA P. CASTELLINO, 111
NAPLES, 80131
ITALY

EXAMINER
ASHEN, JON BENJAMIN

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/604,340	HILDINGER ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-50* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Revised Notice to Comply*.

DETAILED ACTION

Objections to the Specification

Sequence Compliance

The disclosure is objected to because of the following: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification as filed contains numerous instances which do not comply with the requirements above, in particular 1.821(d) at least, wherein numerous nucleotide sequences are set forth without accompanying sequence identifiers. By way of example, Applicant's attention is drawn to pages 186 to 215 of the instant specification which sets forth multiple nucleotide sequences which are shown without accompanying sequence identifiers (SEQ ID NO:).

The above listing of pages is by way of illustration. In order to be fully responsive to this Office Action, Applicant should review this application in its entirety to ensure compliance with the requirements of 37 CFR 1.821 through 1.825 and to make all appropriate corrections.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9, 12, 13-18, 20-21, 24-25, 28-39 and 49-50, drawn to an *in vivo* method of decreasing the expression of a target gene in a mammalian cell comprising administering a recombinant adeno-associated viral vector (rAAV vector) that comprises an RNAi expression cassette as set forth in claims 1 or 2, classifiable in class 514, subclass 44.

II. Claims 10-11, 19, 22-23, 26-27 and 40-48 drawn to a composition comprising a recombinant adeno-associated viral vector (rAAV vector) that comprises an RNAi expression cassette as set forth in claim 1, classifiable in class 536, subclass 24.5.

The inventions are distinct, each from the other because of the following reasons:

2. Groups I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). Invention I is drawn to a method of inhibiting gene expression in mammalian cells, *in vivo*. Invention II is drawn to a pharmaceutical composition comprising a rAAV vector that comprises an RNAi expression cassette. In the instant case the product as claimed can be used in a materially different process of using that product which would be a method of determining gene function in Drosophila cells, *in vitro*.

Furthermore, searching Groups I and II together would impose a serious search burden. In the instant case, a prior art search of methods of *in vivo* treatment comprising administration of an rAAV vector would not be coextensive with a prior art search for the rAAV vector alone. Search of each of these inventions would require different key word searches of the composition and method and would require, at least, a search for the distinctive steps required by the method that would not be required by the composition. These searches would require the use of divergent patent and non-patent literature databases and would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious and undue burden on the Office in terms of both search and examination. As such, it would be burdensome to perform examination of Groups I and II together.

3. Group I is further restricted as follows:

4. Group I comprises claims to the following patentably distinct inventions. Group I comprises claims drawn to methods of treating mammals comprising a) administering an rAAV vector that expresses a short interfering RNA, b) administering at least 2 rAAV vectors that express a short interfering RNA(s) and c) administering an rAAV vector that expresses a short hairpin RNA(s). Each of these methods is patentably distinct because each requires the use of rAAV vectors that express RNAs that are biologically, functionally, structurally and/or chemically distinct. If Applicant chooses to elect group I, the claims of the elected group will be examined insofar as they read on the elected subject matter that is identified above in a, b or c.

5. If applicant chooses to elect invention a or b (as identified above) from group I, Applicant is further required, pursuant to 35 U.S.C. 121 and 37 C.F.R. 1.141, to elect a single RNAi target sequence as listed in claim 36 (that are rhodopsin, ccr5, cxcr4, vegf, HIF or "any other gene of interest") because these sequences are subject to restriction.

The Commissioner has partially waived the requirements of 37 C.F.R. 1.141 and will permit a reasonable number of such nucleotide sequences to be claimed in a single application. Under this policy, up to 10 of independent and distinct nucleotide sequences will be examined in a single application. (see MPEP 803.04 and 2434)

Claim 36 is generic to inventions a and b in group I and is subject to an additional restriction since it is not considered to be a proper genus/Markush. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention

exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claim 36 specifically claims the RNAi target sequences antisense sequences as listed, the expression of which is modulated by the rAAV vectors that are administered by the methods of the invention. The target sequences claimed are considered to be unrelated, since each target sequence claimed is structurally and functionally independent and distinct for the following reasons: each target sequence has a unique nucleotide sequence, each target sequence is targeted by a different and specific RNA and each target sequence, absent evidence to the contrary, will be modulated to varying degrees upon being bound by a different and specific RNA. As such the Markush/genus of RNA target sequences in claim 36 is not considered to constitute a proper genus, and is therefore subject to restriction.

Furthermore, a search of more than one (1) of the RNA target sequences claimed in claim 36 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed antisense sequences. MPEP 808.02 states in part: Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(C) - 806.05(i), the examiner, in order to establish reasons for insisting upon restriction, must shown by appropriate explanation one of the following:

(C) A different field of search: Where it is necessary to search for one of the distinct subjects in places where no pertinent art to the other subject exists, a different field of search is shown, even though the two are classified together.

It is noted that a search of the available sequence databases produces a listing of references disclosing the sequence most similar to the query sequence. This is the "place" where the examiner searches for prior art. The prior art relating to another query sequence will not be found in this "place"- a different listing of references must be generated and searched by the examiner. Thus a different search is shown, and restriction is proper.

In view of the foregoing, one (1) RNA target sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicant is required, if electing invention a or b from group I, to elect one (1) RNA target gene from claim 36 for examination on the merits. Note that this is not a species election.

6. Claims 1 and 2 link(s) inventions of group I that are identified in section 4 above as a, b or c. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1 and 2. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C.

121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

7. This application contains claims directed to the following patentably distinct species of the claimed invention: the species of promoters recited in claims 32-34 that are pol I, pol II and pol III.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 32-34 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record

showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

8. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See

"Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jba

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